Amendments to the Specification:

Applicants request entry of this Sequence Listing into the application in adherence with 37 C.F.R. §§1.821 to 1.825 beginning on page 176, after the Abstract. No new matter has been included.

On pages 3 to 4, paragraph 14, please replace the existing paragraph with the following amended paragraph:

[0014] In one embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of M^1X_nTPLGP or $M^1B_oPZ_mX_nTPLGP$. In this embodiment, the superscript, 1, denotes the first position of the amino acid sequence of the wild-type G-CSF sequence (SEQ ID NO:~~3~~143), the subscripts n and m are integers selected from 0 to 3, and at least one of X and B is threonine or serine, and when more than one of X and B is threonine or serine, the identity of these moieties is independently selected. Also in this embodiment, Z is selected from glutamate, any uncharged amino acid or dipeptide combination including MQ, GQ, and MV. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of MVTPLGP (SEQ ID NO:1), MQTPLGP (SEQ ID NO:2), MIATPLGP (SEQ ID NO:3), MATPLGP (SEQ ID NO:4), MPTQGAMPLGP (SEQ ID NO:5) , MVQTPLGP (SEQ ID NO:6), MQSTPLGP (SEQ ID NO:7), MGQTPLGP (SEQ ID NO:8), MAPTSSSPLGP (SEQ ID NO:9), and MAPTPLGPA (SEQ ID NO:10).

On pages 4 to 5, paragraphs 15, 16, 17, and 18 please replace the existing paragraphs with the following amended paragraphs:

[0015] In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of M^1TPXBO_rP. In this embodiment the superscript, 1, denotes the first position of the amino acid sequence of the wild-type G-CSF sequence (SEQ ID NO:~~3~~ 143), and the subscript r is an integer selected from 0 to 3, and at least one of X, B and O is threonine or serine, and when more than one of X, B and O is threonine or serine, the identity of these moieties is independently selected. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: MTPTLGP (SEQ ID NO:4),

MTPTQLGP (SEQ ID NO:11), MTPTSLGP (SEQ ID NO:12), MTPTQGP (SEQ ID NO:13), MTPTSSP (SEQ ID NO:14), M^1TPQTP (SEQ ID NO:15), M^1TPTGP (SEQ ID NO:16), M^1TPLTP (SEQ ID NO:17), M^1TPNTGP (SEQ ID NO:18), MTPLGP (SEQ ID NO:19), M^1TPVTP (SEQ ID NO:20), M^1TPMVTP (SEQ ID NO:21), and $MT^1P^2TQGL^3G^4P^5A^6S^7$ (SEQ ID NO:22).

[0016] In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of $LGX^{53}B_oLGI$, wherein the superscript denotes the position of the amino acid in the wild type G-CSF amino acid sequence, and X is histidine, serine, arginine, glutamic acid or tyrosine, and B is either threonine or serine, and o is an integer from 0 to 3. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: LGHTLGI (SEQ ID NO:23), LGSSLGI (SEQ ID NO:24), LGYSLGI (SEQ ID NO:25), LGESLGI (SEQ ID NO:26), and LGSTLGI (SEQ ID NO:27).

[0017] In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of $P^{129}Z_mJ_qO_rX_nPT$ wherein the superscript denotes the position of the amino acid in the wild type G-CSF amino acid sequence, and Z, J, O and X are independently selected from threonine or serine, and m, q, r, and n are integers independently selected from 0 to 3. In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: P^{129}ATQPT (SEQ ID NO:28), P^{129}TLGPT (SEQ ID NO:29), P^{129}TQGPT (SEQ ID NO:30), P^{129}TSSPT (SEQ ID NO:31), P^{129}TQGAPT (SEQ ID NO:32), P^{129}NTGPT (SEQ ID NO:33), PALQPTQT (SEQ ID NO:34), P^{129}ALTPT (SEQ ID NO:35), P^{129}MVTPT (SEQ ID NO:36), P^{129}ASSTPT (SEQ ID NO:37), P^{129}TTQP (SEQ ID NO:38), P^{129}NTLP (SEQ ID NO:39), P^{129}TLQP (SEQ ID NO:40), MAP^{129}ATQPTQGAM (SEQ ID NO:41), and MP^{129}ATTQPTQGAM (SEQ ID NO:42).

[0018] In another embodiment, the G-CSF polypeptide comprises a mutant peptide sequence with the formula of $PZ_mU_sJ_qP^{61}O_rX_nB_oC$ wherein the superscript denotes the position of the amino acid in the wild type G-CSF amino acid sequence, and at least one of Z, J, O, and U is selected from threonine or serine, and when more than one of Z, J, O and U is threonine or serine, each is independently selected, X and B are any uncharged amino acid or glutamate, and m, s, q, r, n, and o are integers independently selected from 0 to 3. In another embodiment the

G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: P^{61}TSSC (SEQ ID NO:43), P^{61}TSSAC (SEQ ID NO:44), LGIPTA P^{61}LSSC (SEQ ID NO:45), LGIPTQ P^{61}LSSC (SEQ ID NO:46), LGIPTQG P^{61}LSSC (SEQ ID NO:47), LGIPQT P^{61}LSSC (SEQ ID NO:48), LGIPTS P^{61}LSSC (SEQ ID NO:49), ~~LGIPTS P^{61}LSSC,~~ LGIPTQP^{61}LSSC (SEQ ID NO:50), LGTPWAP^{61}LSSC (SEQ ID NO:51), LGTPFA P^{61}LSSC (SEQ ID NO:52), P^{61}FTP (SEQ ID NO:53), and SLGAP^{58}TAP^{61}LSS (SEQ ID NO:54).

On page 5 paragraphs 19, 20, and 22, please replace the existing paragraphs with the following amended paragraphs:

[0019] In another embodiment the G-CSF polypeptide comprises a mutant peptide sequence with the formula of $Ø_aG_pJ_qO_rP^{175}X_nB_oZ_mU_s\Psi_t$ wherein the superscript denotes the position of the amino acid in SEQ ID NO:~~3~~ 143, and at least one of Z, U, O, J, G, Ø, B and X is threonine or serine and when more than one of Z, U, O, J, G, Ø, B and X are threonine or serine, they are independently selected. Ø is optionally R, and G is optionally H. The symbol Ψ represents any uncharged amino acid residue or glutamate, and a, p, q, r, n, o, m, s, and t are integers independently selected from 0 to 3. In another embodiment the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: RHLAQTP^{175} (SEQ ID NO:55) RHLAGQTP^{175} (SEQ ID NO:56), QP^{175}TQGAMP (SEQ ID NO:57), RHLAQTP^{175}AM (SEQ ID NO:58), QP^{175}TSSAP (SEQ ID NO:59), QP^{175}TSSAP (SEQ ID NO:60), QP^{175}TQGAMP (SEQ ID NO:61), QP^{175}TQGAM (SEQ ID NO:62), QP^{175}TQGA (SEQ ID NO:63), QP^{175}TVM (SEQ ID NO:64), QP^{175}NTGP (SEQ ID NO:65), and QP^{175}QTLP (SEQ ID NO:66).

[0020] In another embodiment the G-CSF polypeptide comprises a mutant peptide sequence selected from the sequences P^{133}TQTAMP^{139} (SEQ ID NO:67) P^{133}TQGTMP (SEQ ID NO:68), P^{133}TQGTNP (SEQ ID NO:69), P^{133}TQGTLP (SEQ ID NO:70), and PALQP^{133}TQTAMPA (SEQ ID NO:71).

[0022] In one embodiment, the hGH polypeptide comprises a mutant peptide sequence with the formula of P^{133}JXBOZUK^{140}QTYS, wherein superscripts denote the position of the amino acid in (SEQ ID NO:~~20~~160); and J is selected from threonine and arginine; X is selected from

alanine, glutamine, isoleucine, and threonine; B is selected from glycine, alanine, leucine, valine, asparagine, glutamine, and threonine; O is selected from tyrosine, serine, alanine, and threonine; and Z is selected from isoleucine and methionine; and U is selected from phenylalanine and proline. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: PTTGQIFK (SEQ ID NO:72), PTTAQIFK (SEQ ID NO:73), PTTLQIFK (SEQ ID NO:74), PTTLYVFK (SEQ ID NO:75), PTTVQIFK (SEQ ID NO:76), PTTVSIFK (SEQ ID NO:77), PTTNQIFK (SEQ ID NO:78), PTTQQIFK (SEQ ID NO:79), PTATQIFK (SEQ ID NO:80), PTQGQIFK (SEQ ID NO:81), PTQGAIFK (SEQ ID NO:82), PTQGAMFK (SEQ ID NO:83), PTIGQIFK (SEQ ID NO:84), PTINQIFK (SEQ ID NO:85), PTINTIFK (SEQ ID NO:86), PTILQIFK (SEQ ID NO:87), PTIVQIFK (SEQ ID NO:88), PTIQQIFK (SEQ ID NO:89), PTIAQIFK (SEQ ID NO:90), P^{133}TTTQIFK^{140}QTYS (SEQ ID NO:91), and P^{133}TQGAMPK^{140}QTYS (SEQ ID NO:92).

On pages 6 to 7, paragraphs 23, 24, 25, 26, 27, and 29, please replace the existing paragraphs with the following amended paragraphs:

[0023]In another embodiment, the hGH polypeptide comprises a mutant peptide sequence with the formula of P^{133}RTGQIPTQBYS wherein superscripts denote the position of the amino acid in SEQ ID NO:~~20~~ 160; and B is selected from alanine and threonine. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: PRTGQIPTQTYS (SEQ ID NO:93) and PRTGQIPTQAYS (SEQ ID NO:94).
[0024] In another embodiment, the hGH polypeptide comprises a mutant peptide sequence with the formula of L^{128}XTBOP^{133}UTG wherein superscripts denote the position of the amino acid inSEQ ID NO:20; and X is selected from glutamic acid, valine and alanine; B is selcted from glutamine, glutamic acid, and glycine; O is selcted from serine and threonine; and U is selected from arginine, serine, alanine and leucine. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: LETQSP^{133}RTG (SEQ ID NO:95), LETQSP^{133}STG (SEQ ID NO:96), LETQSP^{133}ATG (SEQ ID NO:97), LETQSP^{133}LTG (SEQ ID NO:98), LETETP^{133}R (SEQ ID NO:99), LETETP^{133}A (SEQ ID

DB2/20914938.1

NO:100), LVTQSP^{133}RTG (SEQ ID NO:101), LVTETP^{133}RTG (SEQ ID NO:102), LVTETP^{133}ATG (SEQ ID NO:103), and LATGSP^{133}RTG (SEQ ID NO:104).

[0025] In another embodiment the hGH polypeptide comprises a mutant peptide sequence with the formula of $M^1BPTX_nZ_mOPLSRL$ wherein the superscript 1, denotes the position of the amino acid in SEQ ID NO:~~19~~ 159; and B is selected from phenylalanine, valine and alanine or a combination thereof; X is selected from glutamate, valine and proline Z is threonine; O is selected from leucine and isoleucine; and when X is proline, Z is threonine; and wherein n and m are integers selected from 0 and 2. In another embodiment, the hGH polypeptide comprises a mutant peptide sequence selected from the sequences consisting of: M^{1}FPTE IPLSRL (SEQ ID NO:105), M^{1}FPTV LPLSRL (SEQ ID NO:106), and M^{1}APTPTIPLSRL (SEQ ID NO:107).

[0026] In still another embodiment the the hGH polypeptide comprises the following mutant peptide sequence: M^{1}VTPTIPLSRL (SEQ ID NO:108).

[0027] In still another embodiment the hGH polypeptide comprises a mutant peptide sequence selected from M^{1}APTSSPTIPL^{7}SR^9 (SEQ ID NO:109) and DGSP^{133}NTGQIFK^{140} (SEQ ID NO:110).

[0029] In one embodiment, the INF alpha polypeptide has a peptide sequence comprising a mutant amino acid sequence, and the peptide sequence corresponds to a region of INF alpha 2 having a sequence as shown in SEQ NO:~~22~~180, and wherein the mutant amino acid sequence contains a mutation at a position corresponding to T^{106} of INF alpha 2. In another embodiment the IFN alpha polypeptide is selected from the group consisting of IFN alpha, IFN alpha 4, IFN alpha 5, IFN alpha 6, IFN alpha 7, IFN alpha 8, IFN alpha 10, IFN alpha 14, IFN alpha 16, IFN alpha 17, and IFN alpha 21. In yet another embodiment, the IFN alpha polypeptide is an IFN alpha polypeptide comprising a mutant amino acid sequence selected from the group consisting of: ^{99}CVMQEERVTETPLMNADSIL^{118} (SEQ ID NO:111) ^{99}CVMQEEGVTETPLMNADSIL^{118} (SEQ ID NO:112), and ^{99}CVMQGVGVTETPLMNADSIL^{118} (SEQ ID NO:113). In still another embodiment, the IFN alpha polypeptide is an IFN alpha 4 polypeptide comprising a mutant amino acid sequence selected from the group consisting of: ^{99}CVIQEVGVTETPLMNVDSIL^{118} (SEQ ID NO:114), and ^{99}CVIQGVGVTETPLMKEDSIL^{118} (SEQ ID NO:115). In another embodiment, the IFN alpha polypeptide is an IFN alpha 5 polypeptide comprising a mutant

amino acid sequence selected from the group consisting of: ^{99}CMMQEVGVTDTPLMNVDSIL^{118}(SEQ ID NO:116), ^{99}CMMQEVGVTETPLMNVDSIL^{118} (SEQ ID NO:117) and ^{99}CMMQGVGVTDTPLMNVDSIL^{118} (SEQ ID NO:118). In an another embodiment, the IFN alpha polypeptide is an IFN alpha 6 polypeptide comprising a mutant amino acid sequence selected from the group consisting of: ^{99}CVMQEVWVTGTPLMNEDSIL^{118} (SEQ ID NO:119), ^{99}CVMQEVGVTGTPLMNEDSIL^{118} (SEQ ID NO:120) and ^{99}CVMQGVGVTETPLMNEDSIL^{118} (SEQ ID NO:121). In yet an another embodiment, the IFN alpha polypeptide is an IFN alpha 7 polypeptide comprising a mutant amino acid sequence selected from the group consisting of: ^{99}CVIQEVGVTETPLMNEDFIL^{118} (SEQ ID NO:122), and ^{99}CVIQGVGVTETPLMNEDFIL^{118} (SEQ ID NO:123). In still another embodiment, the IFN alpha polypeptide is an IFN alpha 8 polypeptide comprising a mutant amino acid sequence selected from the group consisting of: ^{99}CVMQEVGVTESPLMYEDSIL^{118} (SEQ ID NO:124), and ^{99}CVMQGVGVTESPLMYEDSIL^{118} (SEQ ID NO:125). In another embodiment, the IFN alpha polypeptide is an IFN alpha 10 polypeptide comprising a mutant amino acid sequence selected from the group consisting of: ^{99}CVIQEVGVTETPLMNEDSIL^{118} (SEQ ID NO:126) and ^{99}CVIQGVGVTETPLMNEDSIL^{118} (SEQ ID NO:127). In another embodiment, the IFN alpha polypeptide is an IFN alpha 14 polypeptide comprising a mutant amino acid sequence selected from the group consisting of: ^{99}CVIQEVGVTETPLMNEDSIL^{118} (SEQ ID NO:128), and ^{99}CVIQGVGVTETPLMNEDSIL^{118} (SEQ ID NO:129). In another embodiment, the IFN alpha polypeptide is an IFN alpha 16 polypeptide comprising a mutant amino acid sequence selected from the group consisting of: ^{99}CVTQEVGVTEIPLMNEDSIL^{118} (SEQ ID NO:130), ^{99}CVTQEVGVTETPLMNEDSIL^{118} (SEQ ID NO:131), and ^{99}CVTQGVGVTETPLMNEDSIL^{118} (SEQ ID NO:132). In still another embodiment, the IFN alpha polypeptide is an IFN alpha 17 polypeptide comprising a mutant amino acid sequence selected from the group consisting of: ^{99}CVIQEVGMTETPLMNEDSIL^{118} (SEQ ID NO:133), ^{99}CVIQEVGVTETPLMNEDSIL^{118} (SEQ ID NO:134), and ^{99}CVIQGVGMTETPLMNEDSIL^{118} (SEQ ID NO:135). In one more embodiment, the IFN alpha polypeptide is an IFN alpha 21 polypeptide comprising a mutant amino acid sequence selected from the group consisting of:

^{99}CVIQEVGVTETPLMNVDSIL^{118} (SEQ ID NO:136), and ^{99}CVIQGVGVTETPLMNVDSIL^{118} (SEQ ID NO:137).

On pages 32 to 33, paragraph 133, please replace the existing paragraph with the following amended paragraph:

[0133] One example of this is the glycosylation of the cancer-associated mucin MUC1. MUC1 contains a tandem repeat O-linked glycosylated region of 20 residues (HGVTSAPDTRPAPGSTAPPA (SEQ ID NO:138)) with five potential O-linked glycosylation sites. GalNAc-T1, -T2, and -T3 can initiate glycosylation of the MUC1 tandem repeat and incorporate at only three sites (HGVTSAPDTRPAPGSTAPPA (SEQ ID NO:139), GalNAc attachment sites underlined). GalNAc-T4 is unique in that it is the only GalNAc-transferase isoform identified so far that can complete the O-linked glycan attachment to all five acceptor sites in the 20 amino acid tandem repeat sequence of the breast cancer associated mucin, MUC1. GalNAc-T4 transfers GalNAc to at least two sites not used by other GalNAc-transferase isoforms on the GalNAc$_4$TAP24 glycopeptide (TAPPAHGVTSAPDTRPAPGSTAPP (SEQ ID NO:140), unique GalNAc-T4 attachment sites are in bold) (Bennett et al., *J. Biol. Chem.* **273**: 30472-30481 (1998). An activity such as that exhibited by GalNAc-T4 appears to be required for production of the glycoform of MUC1 expressed by cancer cells where all potential sites are glycosylated (Muller et al., *J. Biol. Chem.* **274**: 18165-18172 (1999)). Normal MUC1 from lactating mammary glands has approximately 2.6 O-linked glycans per repeat (Muller et al., *J. Biol. Chem.* **272**: 24780-24793 (1997) and MUC1 derived from the cancer cell line T47D has 4.8 O-linked glycans per repeat (Muller et al., *J. Biol. Chem.* **274**: 18165-18172 (1999)). The cancer-associated form of MUC1 is therefore associated with higher density of O-linked glycan occupancy and this is accomplished by a GalNAc-transferase activity identical to or similar to that of GalNAc-T4.

On pages 34 to 37, paragraph 138, please replace the existing paragraph with the following amended paragraph:

[0138] epresentative wild type and mutant G-CSF polypeptides have sequences that are selected from:

SEQ. ID NO. ~~1~~ 141(178 amino acid wild type)

mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklvseca tyklchpeel
vllghslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp
elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr
aggvlvashl qsflevsyrv lrhlaqp;

SEQ. ID NO. ~~2~~ 142(178 amino acid wild type without N-terminal methionine)

tplgpasslp qsfllkcleq vrkiqgdgaa lqeklvseca tyklchpeel
vllghslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp
elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr
aggvlvashl qsflevsyrv lrhlaqp;

SEQ. ID NO. ~~3~~ 143(175 amino acid wild type)

mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklca tyklchpeel
vllghslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp
elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr
aggvlvashl qsflevsyrv lrhlaqp;

SEQ. ID NO. 4 144(175 amino acid wild type without N-terminal methionine)

mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklca tyklchpeel
vllghslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp
elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr
aggvlvashl qsflevsyrv lrhlaqp;

SEQ. ID NO. ~~5~~ 145

mvtplgpasslp qsfllkcleq vrkiqgdgaa lqeklca tyklchpeel
vllghslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp

elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr aggvlvashl qsflevsyrv lrhlaqp;

SEQ. ID NO. ~~6~~ <u>146</u>

mvtplgpasslp qsfllkcleq vrkiqgdgaa lqeklca tyklchpeel vllghtlgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr aggvlvashl qsflevsyrv lrhlaqp;

SEQ. ID NO. ~~7~~ <u>147</u>

mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklca tyklchpeel vllghtlgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr aggvlvashl qsflevsyrv lrhlaqp;

SEQ. ID NO. ~~8~~ <u>148</u>

mvtplgpasslp qsfllkcleq vrkiqgdgaa lqeklca tyklchpeel vllgsslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr aggvlvashl qsflevsyrv lrhlaqp;

SEQ. ID NO. ~~9~~ <u>149</u>

mqtplgpasslp qsfllkcleq vrkiqgdgaa lqeklca tyklchpeel vllghslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr aggvlvashl qsflevsyrv lrhlaqp;

SEQ. ID NO. ~~10~~ <u>150</u>

mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklca tyklchpeel vllghslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr aggvlvashl qsflevsyrv lrhlaqptqgamp; and

SEQ. ID NO. ~~11~~ 151

mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklca tyklchpeel
vllgsslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp
elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr
aggvlvashl qsflevsyrv lrhlaqp

SEQ ID NO:~~12~~ 152

maitplgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll
ghslgipwap lsscpsqalq lagclsqlhs glflyqgllq alegispelg
ptldtlqldv adfattiwqq meelgmapal qptqgampaf asafqrragg
vlvashlqsf levsyrvlrh laqp

SEQ ID NO:~~13~~ 153

mgvtetplgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll
ghslgipwap lsscpsqalq lagclsqlhs glflyqgllq alegispelg
ptldtlqldv adfattiwqq meelgmapal qptqgampaf asafqrragg
vlvashlqsf levsyrvlrh laqp

SEQ ID NO:~~14~~ 154

maptplgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll
ghslgipwap lsscpsqalq lagclsqlhs glflyqgllq alegispelg
ptldtlqldv adfattiwqq meelgmapal qptqgampaf asafqrragg
vlvashlqsf levsyrvlrh laqp

SEQ ID NO:~~15~~ 155

Mtptqglgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll
ghslgipwap lsscpsqalq lagclsqlhs glflyqgllq alegispelg
ptldtlqldv adfattiwqq meelgmapal qptqgampaf asafqrragg
vlvashlqsf levsyrvlrh laqp

SEQ ID NO:~~16~~ 156

mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll ghslgipwap lsscpsqalq lagclsqlhs glflyqgllq alegispelg ptldtlqldv adfattiwqq meelgmapatqptqgampaf asafqrragg vlvashlqsf levsyrvlrh laqp

SEQ ID NO:~~17~~ 157

Mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll ghslgipftp lsscpsqalq lagclsqlhs glflyqgllq alegispelg ptldtlqldv adfattiwqq meelgmapaL qptqgampaf asafqrragg vlvashlqsf levsyrvlrh laqp

SEQ ID NO:~~18~~ 158

mtplgpasslpqsfllkcleqvrkiqgdgaalqeklcatyklchpeelvllghslgipw aplsscpsqalqlagclsqlhsglflyqgllqalegispelgptldtlqldvadfattiwqq meelgmapalqptqtampafasafqrraggvlvashlqsflevsyrvlrhlaqp.

On page 38 paragraphs 140 and 141, please replace the existing paragraphs with the following amended paragraphs:

[0140] Representative wild type and mutant hGH polypeptides have sequences that are selected from:

SEQ ID NO:~~19~~ 159 (192 amino acid wild-type pituitary derived hGH comprising an N-terminal methionine)

mfptiplsrlfdnamlrahrlhqlafdtyqefeeayipkeqkysflqnpqtslcfsesipt psnreetqqksnlellrisllliqswlepvqflrsvfanslvygasdsnvydllkdleegi qtlmgrledgsprtgqifkqtyskfdtnshnddallknygllycfrkdmdkvetflriv qcrsvegscgf

SEQ ID NO:~~20~~ 160 (191 amino acid wild-type pituitary derived hGH lacking an N-Terminal methionine)

fptiplsrlfdnamlrahrlhqlafdtyqefeeayipkeqkysflqnpqtslcfsesiptp
snreetqqksnlellrisllliqswlepvqflrsvfanslvygasdsnvydllkdleegiqt
lmgrledgsprtgqifkqtyskfdtnshnddallknygllycfrkdmdkvetflrivqc
rsvegscgf

SEQ ID NO: ~~21~~ 159 (wild type)

MFPTIPLSRLFDNAMLRAHRLHQLAFDTYQEFEEAYIPK
EQKYSFLQNPQTSLCFSESIPTPSNREETQQKSNLELLRIS
LLLIQSWLEPVQFLRSVFANSLVYGASDSNVYDLLKDL
EEGIQTLMGRLEDGSPRTGQIFKQTYSKFDTNSHNDDAL
LKNYGLLYCFRKDMDKVETFLRIVQCRSVEGSCGF

[0141] The following are representative mutant peptide sequences corresponding to the region underlined in the wild type SEQ ID NO:~~21~~ 159: LEDGSP**T**TGQIFKQTYS (SEQ ID NO:161), LEDGSP**T**T**A**QIFKQTYS (SEQ ID NO:162), LEDGSP**TAT**QIFKQTYS (SEQ ID NO:163), LEDGSP**TQ**GA**M**FKQTYS (SEQ ID NO:164), LEDGSP**TQ**GAIFKQTYS (SEQ ID NO:165), LEDGSP**TQ**GQIFKQTYS (SEQ ID NO:166), LEDGSP**TTLYV**FKQTYS (SEQ ID NO:167), LEDGSP**TINT**IFKQTYS (SEQ ID NO:168), LEDGSP**TTVS**IFKQTYS (SEQ ID NO:169), LEDGSPRTGQI**PT**QTYS (SEQ ID NO:170), LEDGSPRTGQI**PT**QAYS (SEQ ID NO:171), LEDGSP**TTL**QIFKQTYS (SEQ ID NO:172), LE**TET**PRTGQIFKQTYS (SEQ ID NO:173), L**VTET**PRTGQIFKQTYS (SEQ ID NO:174), LE**TQ**SPRTGQIFKQTYS (SEQ ID NO:175), L**VTQ**SPRTGQIFKQTYS (SEQ ID NO:176), **LVTET**P**A**TGQIFKQTYS (SEQ ID NO:177), LEDGSP**TQGAMP**KQTYS (SEQ ID NO:178), and LEDGSP**T**T**T**QIFKQTYS (SEQ ID NO:179).

On page 39 paragraph 143, please replace the existing paragraph with the following amended paragraph:

[0143] A wild type and mutant IFN alpha polypeptide is shown below:

SEQ ID NO:~~22~~ 180 (from wild type IFN 2b)

^{98}CVIQGVGVTETPLMKEDSIL^{117}

On pages 136 to 137, paragraphs 518, 519, and 520 please replace the existing paragraphs with the following amended paragraphs:

[0518] This example discloses amino acid sequence mutations that introduce changes introduce O-linked glycosylation sites, *i.e.*, serine or threonine residues, into a preferably proline-containing site in the 175 amino acid wild-type sequence of G-CSF or any modified version thereof. As a reference the 175 amino acid wild-type G-CSF sequence is shown below:

MTPLGPASSLP QSFLLKCLEQ VRKIQGDGAA LQEKLCA TYKLCHPEEL VLLGHSLGIP WAPLSSCPSQ ALQLAGCLSQ LHSGLFLYQG LLQALEGISP ELGPTLDTLQ LDVADFATTI WQQMEELGMA PALQPTQGAM PAFASAFQRR AGGVLVASHL QSFLEVSYRV LRHLAQP **(SEQ ID NO:~~2~~ 143)**

3.1 N-terminal Mutations

[0519] In the N-terminal mutants, the N-terminus of a wild-type G-CSF, M^{1}TPLGPA (SEQ ID NO:181), is replaced with either M^{1}X$_n$TPLGPA or M^{1}B$_o$PZ$_m$X$_n$TPLGPA. Wherein n, o and m are integers slected from 0 to 3, and at least one of X, B and O is Thr or Ser. When more than one of X, B and O is Thr or Ser, the identity of these moieties is independently selected. Where they appear, superscripts denote the position of the amino acid in the wild-type starting sequence.

[0520] Preferred examples include:

M^{1}VTPL^{4}GPA (SEQ ID NO:182)
M^{1}QTPL^{4}GPA (SEQ ID NO:183)
M^{1}ATPL^{4}GPA (SEQ ID NO:184)
M^{1}PTQGAMPL^{4}GPA (SEQ ID NO:185)
M^{1}VQTPL^{4}GPA (SEQ ID NO:186)
M^{1}QSTPL^{4}GPA (SEQ ID NO:187)
M^{1}GQTPL^{4}GPA (SEQ ID NO:188)

M^{1}APTSSSPL^{4}GPA (SEQ ID NO:189)

M^{1}APTPL^{4}GPA (SEQ ID NO:10)

On page 137 paragraphs 521, 522, 523, and 524, please replace the existing paragraphs with the following amended paragraphs:

[0521] In these mutants, the N-terminus of a wild-type GCSF, **M^{1}TPLGP** (SEQ ID NO:~~8~~ 190), is replaced with **M^{1}TPX$_n$B$_o$O$_r$P**. Wherein n, o and r are integers slected from 0 to 3, and at least one of X, B and O is Thr or Ser. When more than one of X, B and O is Thr or Ser, the identity of these moieties is independently selected. Where they appear, superscripts denote the position of the amino acid in the wild-type starting sequence.

[0522] Preferred mutations include:

M^{1}TPTLGP (SEQ ID NO:~~8~~ 11)

M^{1}TPTQLGP (SEQ ID NO:~~8~~ 12)

M^{1}TPTSLGP (SEQ ID NO:~~8~~ 13)

M^{1}TPTQGP (SEQ ID NO:~~8~~ 14)

M^{1}TPTSSP (SEQ ID NO:~~8~~ 15)

M^{1}TPQTP (SEQ ID NO:~~8~~ 16)

M^{1}TPTGP (SEQ ID NO:~~8~~ 17)

M^{1}TPLTP (SEQ ID NO:~~8~~ 18)

M^{1}TPNTGP (SEQ ID NO:~~8~~ 19)

M^{1}TPVTP (SEQ ID NO:~~8~~ 20)

M^{1}TPMVTP (SEQ ID NO:~~8~~ 21)

MT^{1}P^{2}TQGL^{3}G^{4}P^{5}A^{6}S^7 (SEQ ID NO:~~8~~ 22)

[0523] This mutation is made for the purpose of maintaining G-CSF activity. In these mutants, the amino acid sequence containing H^{53}, **LGH^{53}SLGI** (SEQ ID NO:191) is mutated to **LGH^{53}B$_o$LGI**, where Θ is H, S, R,E or Y, and B is either Thr or Ser.

[0524] Preferred examples include:

LGHTLGI (SEQ ID NO:23)

LGSSLGI (SEQ ID NO:24)

LGYSLGI (SEQ ID NO:25)

LGESLGI (SEQ ID NO:26)

LGSTLGI (SEQ ID NO:27)

On pages 138 to 139, paragraphs 525, 526, 527, and 528, please replace the existing paragraphs with the following amended paragraphs:

[0525] In this type of mutant, the amino acid sequence encompassing P^{129}, **P^{129}ALQPT** (SEQ ID NO:192), is mutated to **$P^{129}Z_mJ_qO_rX_nPT$**, wherein Z, J, O and X are independently selected from Thr or Ser, **and m, q, r, and n are integers slected from 0 to 3.**

[0526] Preferred examples include:

P^{129}TLGPT (SEQ ID NO:29)

P^{129}TQGPT (SEQ ID NO:30)

P^{129}TSSPT (SEQ ID NO:31)

P^{129}TQGAPT (SEQ ID NO:32)

P^{129}NTGPT (SEQ ID NO:33)

P^{129}ALTPT (SEQ ID NO:35)

P^{129}MVTPT (SEQ ID NO:36)

P^{129}ASSTPT (SEQ ID NO:37)

P^{129}TTQP (SEQ ID NO:38)

P^{129}NTLP (SEQ ID NO:39)

P^{129}TLQP (SEQ ID NO:40)

MAP^{129}ATQPTQGAM (SEQ ID NO:41)

MP^{129}ATTQPTQGAM (SEQ ID NO:42)

3.5 Internal Mutation Site 4

[0527] In this type of mutant, the amino acid sequence surrounding P^{61}, LGIPWAP^{61}LSSC (SEQ ID NO:213), is replaced with $PZ_mU_sJ_qP^{61}O_rX_nB_oC$, wherein m, s, q, r, n, and o are integers slected from 0 to 3, and at least one of Z, J, O, X, B and U is selected as either Thr or Ser. When more than one of Z, J, O X, B and U is Thr or Ser, each is independently selected

[0528] Preferred examples include:

P^{61}TSSC (SEQ ID NO:43)
P^{61}TSSAC (SEQ ID NO:44)
LGIPTA P^{61}LSSC (SEQ ID NO:45)
LGIPTQ P^{61}LSSC (SEQ ID NO:46)
LGIPTQG P^{61}LSSC (SEQ ID NO:47)
LGIPQT P^{61}LSSC (SEQ ID NO:48)
LGIPTS P^{61}LSSC (SEQ ID NO:49)
~~LGIPTS P^{61}LSSC~~
LGIPTQP^{61}LSSC (SEQ ID NO:50)
LGTPWAP^{61}LSSC (SEQ ID NO:51)
LGTPFA P^{61}LSSC (SEQ ID NO:52)
P^{61}FTP (SEQ ID NO:53)
SLGAP^{58}TAP^{61}LSS (SEQ ID NO:54)

On pages 139 to 140, paragraphs 529, 530, and 531 please replace the existing paragraphs with the following amended paragraphs:

[0529] In this type of mutant, the amino acid sequence at the C-terminus of a wild-type G-CSF, RHLAQP^{175} (SEQ ID NO:193) is replaced with $Ø_aG_pJ_qO_rP^{175}X_nB_oZ_mU_s\Psi_t$, wherein a, p, q, r, n, o, m, s, and t are integers slected from 0 to 3, and at least one of Z, U, O, J, G, Ø, B and X is Thr or Ser and when more than one of Z, U, O, J, G, Ø, B and X are Thr or Ser, they are independently selected. Ø is optionally R, and G is optionally H. The symbol Ψ represents any uncharged amino acid residue or E (glutamate).

[0530] Preferred examples include:

RHLAQTP^{175} SEQ ID NO:55)

RHLAGQTP^{175} (SEQ ID NO:56)

QP^{175}TQGAMP (SEQ ID NO:57)

RHLAQTP^{175}AM (SEQ ID NO:58)

QP^{175}TSSAP (SEQ ID NO:59)

QP^{175}TSSAP (SEQ ID NO:60)

QP^{175}TQGAMP (SEQ ID NO:61)

QP^{175}TQGAM (SEQ ID NO:62)

QP^{175}TQGA (SEQ ID NO:63)

QP^{175}TVM (SEQ ID NO:64)

QP^{175}NTGP (SEQ ID NO:65)

QP^{175}QTLP (SEQ ID NO:66)

[0531] Additional G-CSF mutants include those with internal mutations surrounding the amino acid P^{133}. Examples include:

P^{133}TQTAMP^{139} (SEQ ID NO:67)

P^{133}TQGTMP (SEQ ID NO:68)

P^{133}TQGTNP (SEQ ID NO:69)

P^{133}TQGTLP (SEQ ID NO:70)

PALQP^{133}TQTAMPA (SEQ ID NO:71)

On pages 140 to 141, paragraph 532, please replace the existing paragraph with the following amended paragraph:

[0532] Mutations in the amino acid sequence of granulocyte colony stimulating factor (G-CSF) can introduce additional sites for O-linked glycosylation, such that the protein may be modified at these sites using the method of the present invention. This example sets forth selected representative mutants of the invention.

4.1 G-CSF (wild type 178 aa variant)

mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklvseca tyklchpeel vllghslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr aggvlvashl qsflevsyrv lrhlaqp (SEQ ID NO:~~1~~ 141)

4.2 G-CSF (wild type 175 aa variant)

mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklca tyklchpeel vllghslgip waplsscpsq alqlagclsq lhsglflyqg llqalegisp elgptldtlq ldvadfatti wqqmeelgma palqptqgam pafasafqrr aggvlvashl qsflevsyrv lrhlaqp **(SEQ ID NO:~~3~~ 143)**

4.9 G-CSF Mutant 1 (Amino Terminal mutation)

miatplgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll ghslgipwap lsscpsqalq lagclsqlhs glflyqgllq alegispelg ptldtlqldv adfattiwqq meelgmapal qptqgampaf asafqrragg vlvashlqsf levsyrvlrh laqp (SEQ ID NO:195)

4.10G-CSF Mutant 2 (Amino Terminal mutation)

mgvtetplgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll ghslgipwap lsscpsqalq lagclsqlhs glflyqgllq alegispelg ptldtlqldv adfattiwqq meelgmapal qptqgampaf asafqrragg vlvashlqsf levsyrvlrh laqp (SEQ ID NO:153)

4.11 G-CSF Mutant 3 (Amino Terminal mutation)

maptplgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll ghslgipwap lsscpsqalq lagclsqlhs glflyqgllq alegispelg ptldtlqldv adfattiwqq meelgmapal qptqgampaf asafqrragg vlvashlqsf levsyrvlrh laqp (SEQ ID NO:154)

4.12 G-CSF Mutant 4 (Site 1)

mtp[3]**tqg**lgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll ghslgipwap lsscpsqalq lagclsqlhs glflyqgllq alegispelg ptldtlqldv adfattiwqq meelgmapal qptqgampaf asafqrragg vlvashlqsf levsyrvlrh laqp (SEQ ID NO:155)

4.13 G-CSF Mutant 5 (Site 3)

Mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll ghslgipwap lsscpsqalq lagclsqlhs glflyqgllq alegispelg ptldtlqldv adfattiwqq meelgm**ap**[129]**at qptqgampaf** asafqrragg vlvashlqsf levsyrvlrh laqp (SEQ ID NO:156)

4.14 G-CSF Mutant 6 (Site 4)

Mtplgpasslp qsfllkcleq vrkiqgdgaa lqeklcatyk lchpeelvll ghslgip[58]ftp lsscpsqalq lagclsqlhs glflyqgllq alegispelg ptldtlqldv adfattiwqq meelgmapaL qptqgampaf asafqrragg vlvashlqsf levsyrvlrh laqp (SEQ ID NO:157)

On pages 149 and 150, Table X. which continues on page 150, please replace the existing Table with the following amended Table:

Table X. GalNAc addition of Mutant G-CSF (MW measured by MALDI)

Peptide	MW(Intact material)	MW (GalNAc-adduct)	Number of GalNAc addition
MutantG-CSF-1 (SEQ ID NO:154) (MAPT-G-CSF)	18965	19369	2
MutantG-CSF-2 (SEQ ID NO:156)	18766	19029	1
MutantG-CSF-3 (SEQ ID NO:158)	18822	19026	1
MutantG-CSF-4 (SEQ ID NO:150)	19369	19574	1

MutantG-CSF-5 (SEQ ID NO:194)	18957	18853	1
MutantG-CSF-6 (SEQ ID NO:141)			NT
Native G-CSF (SEQ ID NO:195)	18800	19023	1

On pages 153 to 155, paragraph 568, please replace the existing paragraph with the following amended paragraph:

[0568] MAPTP-G-CSF solution (540 ug) was concentrated and exchanged with 1M MES buffer (pH 6.0) and adjusted to 50 ul. Then UDP-GalNAc (100 ug, 0.15 umol, 5 eq), GalNAcT$_2$ (5.0 U/ml, 5 ul) and 100 mM MnCl$_2$ (5 ul) was added. The resulting mixture was rocked at RT overnight. Then CMP-SA-PEG (20K) (2.16 mg, 0.108 umol) and St$_6$GalNAcI (1.0 U/ml, 50 ul) were added. The solution was rocked at rt for 60h.. Additional CMP-SA-PEG(20K) (2.16 mg , 0.108 umol) and St6GalNAcI (1.0U/ml, 50 ul) were added, followed by slow rotation at rt for 24 h. Reaction mixture was exchanged with buffer A (25 mM NaOAc, 0.005% polysorbate 80, pH 4.5), then purified on an Amersham SP-FF (5 mL) column with an isocratic elution of 100% A for 10 minutes followed by a linear gradient of 100% A to 20 % B over 20 minutes at a flow rate of 3 mL min^{-1}, where B = 25 mM NaOAc, 2 M NaCl 0.005% polysorbate 80, pH 4.5. The peak at retention time 17 mins was pooled and concentrated to 0.5 ml, which was further purified on an Amersham HiLoad Superdex 200 (16 x 600 mm, 34 μm) with phosphate buffered saline, pH 5.0, 0.005% Tween80, at a flow rate of 0.4 mL min^{-1}. Product fractions at retention time 160 mins was pooled, concentrated to provide 30 ug of MAPT-G-CSF(GalNAc-SA-PEG(20K))$_2$(BCA). The yield was not optimized.

12.4 g Sequences of G-CSF mutants

Mutant G-CSF-1:

MAPTPLGPASSLPQSFLLKCLEQVRKIQGDGAALQEKLCATYKLCHPEELVLLGHSLGIP
WAPLSSCPSQALQLAGCLSQLHSGLFLYQGLLQALEGISPELGPTLDTLQLDVADFATTI

WQQMEELGMAPALQPTQGAMPAFASAFQRRAGGVLVASHLQSFLEVSYRVLRHLAQP **(SEQ ID NO: ~~9~~ 154)**

Mutant G-CSF-2:

MTPLGPASSLPQSFLLKCLEQVRKIQGDGAALQEKLCATYKLCHPEELVLLGHSLGIPW
APLSSCPSQALQLAGCLSQLHSGLFLYQGLLQALEGISPELGPTLDTLQLDVADFATTIW
QQMEELGMAPATQPTQGAMPAFASAFQRRAGGVLVASHLQSFLEVSYRVLRHLAQP
(SEQ ID NO:156)

Mutant G-CSF-3:

MTPLGPASSLPQSFLLKCLEQVRKIQGDGAALQEKLCATYKLCHPEELVLLGHSLGIPW
APLSSCPSQALQLAGCLSQLHSGLFLYQGLLQALEGISPELGPTLDTLQLDVADFATTIW
QQMEELGMAPALQPTQTAMPAFASAFQRRAGGVLVASHLQSFLEVSYRVLRHLAQP
(SEQ ID NO:158)

Mutant G-CSF-4 (C-terminal tag):

MTPLGPASSLPQSFLLKCLEQVRKIQGDGAALQEKLCATYKLCHPEELVLLGHSLGIPW
APLSSCPSQALQLAGCLSQLHSGLFLYQGLLQALEGISPELGPTLDTLQLDVADFATTIW
QQMEELGMAPALQPTQGAMPAFASAFQRRAGGVLVASHLQSFLEVSYRVLRHLAQPT
QGAMP **(SEQ ID NO:~~8~~ 150)**

Mutant G-CSF-5 (N-terminal MIATP):

MIATPLGPASSLPQSFLLKCLEQVRKIQGDGAALQEKLCATYKLCHPEELVLLGHSLGIP
WAPLSSCPSQALQLAGCLSQLHSGLFLYQGLLQALEGISPELGPTLDTLQLDVADFATTI
WQQMEELGMAPALQPTQGAMPAFASAFQRRAGGVLVASHLQSFLEVSYRVLRHLAQP
(SEQ ID NO:~~10~~ 194)

Mutant G-CSF-6 (177 Mer):

MTPLGPASSLPQSFLLKCLEQVRKIQGDGAALQEKLVSECATYKLCHPEELVLLGHSLGI
PWAPLSSCPSQALQLAGCLSQLHSGLFLYQGLLQALEGISPELGPTLDTLQLDVADFATT

IWQQMEELGMAPALQPTQGAMPAFASAFQRRAGGVLVASHLQSFLEVSYRVLRHLAQP **(SEQ ID NO:~~1~~ 141)**

Human recombinant G-CSF expressed in E coli:

MTPLGPASSLPQSFLLKCLEQVRKIQGDGAALQEKLCATYKLCHPEELVLLGHSLGIPW APLSSCPSQALQLAGCLSQLHSGLFLYQGLLQALEGISPELGPTLDTLQLDYADFATTIW QQMEELGMAPALQPT^{134}QGAMPAFASAFQRRAGGVLVASHLQSFLEVSYRVLRHLAQP **(SEQ ID NO:~~2~~ 195)**

On pages 155 to 156, paragraph 569, please replace the existing paragraph with the following amended paragraph:

[0569] The following Example illustrates preparation of a GlycoPEGylated hGH protein The wild-type hGH has no natural glycosylation site, therefore a *de novo* O-glycosylation site was engineered into a mutant hGH protein which was then be glycosylated with a GalNAc transferase and sialylPEGylated at the mutant site. Five mutant hGH proteins were designed to incorporate an O-glycosylation site at either the amino terminus or in the loop region of the protein molecule. The five mutant proteins were produced and each was tested for hGH activity in a Nb2-11 cell proliferation assay.

13.1 Mutant hGH Amino Acid Sequences:

192 amino acid Wild-type pituitary derived hGH comprising an N-Terminal methionine

MFPTIPLSRLFDNAMLRAHRLHQLAFDTYQEFEEAYIPKEQKYSFLQNPQT SLCFSESIPTPSNREETQQKSNLELLRISLLLIQSWLEPVQFLRSVFANSLVYGASDSNVYD LLKDLEEGIQTLMGRLEDGSPRTGQIFKQTYSKFDTNSHNDDALLKNYGLLYCFRKDMD KVETFLRIVQCRSVEGSCGF **(SEQ ID NO:159)**

191 amino acid Wild-type pituitary derived hGH lacking an N-Terminal methionine

FPTIPLSRLFDNAMLRAHRLHQLAFDTYQEFEEAYIPKEQKYSFLQNPQTS LCFSESIPTPSNREETQQKSNLELLRISLLLIQSWLEPVQFLRSVFANSLVYGASDSNVYDL LKDLEEGIQTLMGRLEDGSPRTGQIFKQTYSKFDTNSHNDDALLKNYGLLYCFRKDMD KVETFLRIVQCRSVEGSCGF **(SEQ ID NO:160)**

MVTP mutant:

(M)VTPTIPLSRLFDNAMLRAHRLHQLAFDTYQEFEEAYIPKEQKYSFLQN PQTSLCFSESIPTPSNREETQQKSNLELLRISLLLIQSWLEPVQFLRSVFANSLVYGASDSN VYDLLKDLEEGIQTLMGRLEDGSPRTGQIFKQTYSKFDTNSHNDDALLKNYGLLYCFRK DMDKVETFLRIVQCRSVEGSCGF **(SEQ ID NO: 196)**

PTQGAMP mutant:

MFPTIPLSRLFDNAMLRAHRLHQLAFDTYQEFEEAYIPKEQKYSFLQNPQT SLCFSESIPTPSNREETQQKSNLELLRISLLLIQSWLEPVQFLRSVFANSLVYGASDSNVYD LLKDLEEGIQTLMGRLEDGSPTQGAMPKQTYSKFDTNSHNDDALLKNYGLLYCFRKDM DKVETFLRIVQCRSVEGSCGF **(SEQ ID NO:197)**

TTT mutant:

MFPTIPLSRLFDNAMLRAHRLHQLAFDTYQEFEEAYIPKEQKYSFLQNPQT SLCFSESIPTPSNREETQQKSNLELLRISLLLIQSWLEPVQFLRSVFANSLVYGASDSNVYD LLKDLEEGIQTLMGRLEDGSPTTTQIFKQTYSKFDTNSHNDDALLKNYGLLYCFRKDMD KVETFLRIVQCRSVEGSCGF **(SEQ ID NO: 198)**

MAPT mutant:

MAPTSSPTIPLSRLFDNAMLRAHRLHQLAFDTYQEFEEAYIPKEQKYSFLQ NPQTSLCFSESIPTPSNREETQQKSNLELLRISLLLIQSWLEPVQFLRSVFANSLVYGASDS

NVYDLLKDLEEGIQTLMGRLEDGSPRTGQIFKQTYSKFDTNSHNDDALLKNYGLLYCFR KDMDKVETFLRIVQCRSVEGSCGF **(SEQ ID NO: 199)**

NTG mutant:

MFPTIPLSRLFDNAMLRAHRLHQLAFDTYQEFEEAYIPKEQKYSFLQNPQT SLCFSESIPTPSNREETQQKSNLELLRISLLLIQSWLEPVQFLRSVFANSLVYGASDSNVYD LLKDLEEGIQTLMGRLEDGSPNTGQIFKQTYSKFDTNSHNDDALLKNYGLLYCFRKDM DKVETFLRIVQCRSVEGSCGF **(SEQ ID NO: 200)**

On pages 157 and 158, paragraphs 571, 572, 573, 574, and 575 please replace the existing paragraphs with the following amended paragraphs:

[0571] For the TTT mutant (SEQ ID NO: 198), GalNAc addition gave rise to a complex mixture of unglycosylated, and 1-GalNAc and 2-GalNAc species. Peptide mapping experiments (trypsin digest) showed that the two GalNAc's were added to the T12 peptide (L129-K141) containing the TTT mutation. The (M)VTP mutant (SEQ ID NO: 196) showed only a trace of GalNAc added by MALDI-MS.

[0572] The hGH-TTT-mutant (SEQ ID NO: 198) (4.0 mL, 6.0 mg, 0.27 micromoles) was buffer exchanged twice with 15 mL of Washing Buffer (20 mM HEPES, 150 mM NaCl, 0.02% NaN_3, pH 7.4) and once with Reaction Buffer (20 mM HEPES, 150 mM NaCl, 5 mM $MnCl_2$, 5 mM $MgCl_2$, 0.02% NaN_3, pH 7.4) then concentrated to 2.0 mL using a Centricon centrifugal filter, 5 KDa MWCO.

[0573] The hGH-TTT mutant (SEQ ID NO: 198) was combined with UDP-GalNAc (1.38 micromoles, 0.90 mg) and GalNAc-T2 (0.12 mL, 120 mU). The reaction was incubated at 32°C with gentle shaking for 19 hours. The reaction was analyzed by MALDI-MS and partial addition of GalNAc to the hGH-TTT mutant (SEQ ID NO: 198) was observed (approximately 40%). CMP-SA-PEG-30K (16 mg, 0.533 micromoles) and ST6GalNAc1 (0.375 mL, 375 mU) were added to the reaction mixture to bring the total volume to 2.85 mL. The reaction was incubated at 32°C with gentle shaking for 22 h. The reaction was monitored by SDS PAGE at 0 h and 22 h.

The extent of reaction was determined by SDS-PAGE gel. The product, hGH-(TTT)-GalNAc-SA-PEG-30 KDa, was purified using SP Sepharose and analyzed by SDS-PAGE. Very low yield of the desired hGH-(TTT)-GalNAc-SA-PEG-30 KDa was observed.

*13.3 Preparation of hGH-(***PTQGAMP***)-GalNAc-SA-PEG-30KDa.*

[0574] The PTQGAMP mutant (SEQ ID NO: 197) was was readily glycosylated with UDP-GalNAc and GalNAc T2, then GlycoPEGylated using CMP-SA-PEG-30KDa and ST6GalNAc1 on 10 mg scale to yield 1.45 mg of purified hGH-(PTQGAMP)-GalNAc-SA-PEG-30KDa. Peptide mapping experiments (trypsin digest) located the GalNAc on the trypsin T12 peptide (L129-K141) containing the PTQGAMP mutation.

[0575] The hGH-PTQGAMP-mutant (SEQ ID NO: 197) (4.55 mL, 10.0 mg, 0.45 micromoles) was buffer exchanged twice with 15 mL of Washing Buffer (20 mM HEPES, 150 mM NaCl, 0.02% NaN_3, pH 7.4) and once with Reaction Buffer (20 mM HEPES, 150 mM NaCl, 5 mM $MnCl_2$, 5 mM $MgCl_2$, 0.02% NaN_3, pH 7.4) then concentrated to 3 mL using a Centricon centrifugal filter, 5 KDa MWCO.

On page 158 paragraphs 576 and 579, please replace the existing paragraphs with the following amended paragraphs:

[0576] The hGH-PTQGAMP mutant (SEQ ID NO: 197) was combined with UDP-GalNAc (2.26 micromoles, 1.47 mg) and GalNAc-T2 (0.1 mL, 100 mU). The reaction was incubated at 32°C with gentle shaking for 22 hours. The reaction was analyzed by MALDI-MS and complete addition of GalNAc to the hGH-PTQGAMP mutant (SEQ ID NO: 197) was observed. CMP-SA-PEG-30K (27 mg, 0.9 micromoles) and ST6GalNAc1 (0.350 mL, 350 mU) were added to the reaction mixture to bring the total volume to 3.4 mL. The reaction was incubated at 32°C with gentle shaking for 24 h. The reaction was monitored by SDS PAGE at 0 hours and 16.5 hours. The extent of reaction was determined by SDS-PAGE gel. The product, hGH-(PTQGAMP)-GalNAc-SA-PEG-30 KDa, was purified using SP Sepharoseand SEC (Superdex 200) chromatographyand then formulated. The final product was analyzed by MALDI, peptide

map and SDS-PAGE (silver stain). Protein was determined by BCA vs. BSA standard. The overall isolated yield (1.45 mg) was 12.5 % based on protein.

[0579] UDP-Gal (6 mg, 9.8 mmol), core-1-Gal-T_1 (0.5 U/mL, 80 μL), CMP-SA-PEG (20 kilodalton) (6 mg, 0.3 μmol), α-(O)-sialyltransferase (1 U/mL, 120 μL), 100 mM $MnCl_2$ (50 μL) were added. The resulting mixture was slowly rotated at 32° C for 48 h. The reaction mixture was centrifuged at 2 rpm for 5 min. The protein solution was taken. The remain resin was mixed with 1 mL 25 mM MES buffer (pH 6.0) and vibrated for 30 sec. The suspension was concentrated in again; the protein solutions were combined and concentrated to 200 ~~mcL~~ μL. HPLC Purification provided glyco-PEG-ylated GM-CSF.

On page 159 paragraph 580, please replace the existing paragraph with the following amended paragraph:

[0580] An O-linked glycosylation site similar to that of interferon alpha-2 can be incorporated into any interferon alpha protein at the same relative position. This can be performed by aligning the amino acid sequence of interest with the IFN-alpha-2b sequence (10-20 amino acids long) and modifying the amino acid sequence to incorporate the glycosylation site. Mutation with any amino acid, deletion or insertion can be used to create the site. Exemplary mutants maintain as high an homology as possible with the IFN-alpha-2 sequence in this region with an emphasis on the T at position 106 (shown below in bold). An example of how this is performed is shown below.

Alignments of Interferon alpha's in the NCBI Protein Database

GI# **AA#** **AA Sequence** **Name**

IFN-a-2β 1 CVIQGVGV**T**ETPLMKEDSIL 20 **(SEQ ID NO:~~X~~ 180)**

124449 98 .... 117 IFN-alpha 2 (a,b,c) (SEQ ID NO: 180)

20178265	99	....E...E.....N.....	118	IFN-alpha 14 (SEQ ID NO: 202)
124453	99	....E...E.....N.....	118	IFN-alpha 10 (SEQ ID NO: 203)
585316	99	....E..ME.....N.....	118	IFN-alpha 17 (SEQ ID NO: 204)
124442	99	....E...E.....N..F..	118	IFN-alpha 7 (SEQ ID NO: 205)
124438	99	....E...E.....NV....	118	IFN-alpha 4 (SEQ ID NO: 206)
417188	99	..M.E...I.S...Y.....	118	IFN-alpha 8 (SEQ ID NO: 207)
20178289	99	....E...E.....NV....	118	IFN-alpha 21 (SEQ ID NO: 208)
124457	99	.MM.E...ED....NV....	118	IFN-alpha 5 (SEQ ID NO: 209)
124463	99	..T.E...E.IA..N.....	118	IFN-alpha 16 (SEQ ID NO: 210)
124460	99	..M.E.W.GG....N.....	118	IFN-alpha 6 (SEQ ID NO: 211)
124455	99	..M.EER.G.....NA....	118	IFN-alpha 1/13 (SEQ ID NO: 212)

On page 160 and 161 please replace the Table preceding paragraph 583 with the following amended Table:

GI#	AA#	AA Sequence	Name
IFN-a-2β	1	CVIQGVGV**T**ETPLMKEDSIL 20	**(SEQ ID NO:~~X~~ 180)**
124449	98	 117	IFN-alpha 2 (a,b,c) **(SEQ ID NO:180)**
20178265	99	....E...**T**.....N..... 118	IFN-alpha 14 ($E^{107}T$) (SEQ ID NO: 128)
20178265	99	....**G**...**T**.....N..... 118	IFN-alpha 14 ($E^{103}G$; $E^{107}T$) (SEQ ID NO: 129)
124453	99	....E...**T**.....N..... 118	IFN-alpha 10 ($E^{107}T$) (SEQ ID NO: 126)
124453	99	....**G**...**T**.....N..... 118	IFN-alpha 10 ($E^{103}G$; $E^{107}T$) (SEQ ID NO: 127)
585316	99	....E..M**T**.....N..... 118	IFN-alpha 17 ($E^{107}T$) (SEQ ID NO: 133)
585316	99	....E..**VT**.....N..... 118	IFN-alpha 17 ($ME^{107}VT$) (SEQ ID NO: 134)
585316	99	....**G**..M**T**.....N..... 118	IFN-alpha 17 ($E^{103}G$; $E^{107}T$) (SEQ ID NO: 135)
124442	99	....E...**T**.....N..F.. 118	IFN-alpha 7 ($E^{107}T$) (SEQ ID NO: 122)
124442	99	....**G**...**T**.....N..F.. 118	IFN-alpha 7 ($E^{103}G$; $E^{107}T$) (SEQ ID NO: 123)
124438	99	....E...**T**.....NV.... 118	IFN-alpha 4 ($E^{107}T$) (SEQ ID NO: 114)
124438	99	....**G**...**T**.....NV.... 118	IFN-alpha 4 ($E^{103}G$; $E^{107}T$) (SEQ ID NO: 115)
417188	99	..M.E...**T**.S...Y..... 118	IFN-alpha 8 ($I^{107}T$) (SEQ ID NO: 124)

417188 99 ..M.**G**...**T**.S...Y..... 118 IFN-alpha 8 ($E^{103}G$; $I^{107}T$) (SEQ ID NO: 125)

20178289 99 ....E...**T**.....NV.... 118 IFN-alpha 21 ($E^{107}T$) (SEQ ID NO: 136)

20178289 99 ....**G**...**T**.....NV.... 118 IFN-alpha 21 ($E^{103}G$; $E^{107}T$) (SEQ ID NO: 137)

124457 99 .MM.E...**TD**....NV.... 118 IFN-alpha 5 ($E^{107}T$) (SEQ ID NO: 116)

124457 99 .MM.E...**TE**....NV.... 118 IFN-alpha 5 ($ED^{108}TE$) (SEQ ID NO: 117)

124457 99 .MM.**G**...**TD**....NV.... 118 IFN-alpha 5 ($E^{103}G$; $E^{107}T$) (SEQ ID NO: 118)

124463 99 ..T.E...**T**.**IP**..N..... 118 IFN-alpha 16 ($E^{107}T$;$A^{110}P$) (SEQ ID NO: 130)

124463 99 ..T.E...**T**.**TP**..N..... 118 IFN-alpha 16 ($E^{107}T$;$IA^{110}TP$) (SEQ ID NO: 131)

124463 99 ..T.**G**...**T**.**TP**..N..... 118 IFN-alpha 16 ($E^{103}G$;$E^{107}T$;$IA^{110}TP$) (SEQ ID NO: 132)

124460 99 ..M.E.W.**T**G....N..... 118 IFN-alpha 6 ($G^{107}T$) (SEQ ID NO: 119)

124460 99 ..M.E.**G**.**T**G....N..... 118 IFN-alpha 6 ($W^{105}G$;$G^{107}T$) (SEQ ID NO: 120)

124460 99 ..M.**G**.**G**.**TE**....N..... 118 IFN-alpha 6 (E103G;$W^{105}G$;$GG^{108}TE$) (SEQ ID NO: 121)

124455 99 ..M.EER.**T**.....NA.... 118 IFN-alpha 1/13 ($G^{107}T$) (SEQ ID NO: 111)

124455 99 ..M.EE**G**.**T**.....NA.... 118 IFN-alpha 1/13 ($R^{105}G$;$G^{107}T$) (SEQ ID NO: 112)

124455 99 ..M.**GVG.T**.....NA.... 118 IFN-alpha 1/13
(EER^{105}GVG;G^{107}T) (SEQ ID NO: 113)

The GI numbers in the above table, except the first number 124449, refer to those of the unmodified wild-type proteins.